

## AMENDMENTS TO THE CLAIMS

WHAT IS CLAIMED IS:

1. (Currently amended) A method of identifying a candidate RB pathway modulating agent, said method comprising the steps of:
  - (a) providing an assay system comprising a PSMC 26S protease regulatory subunit C2 (PSMC2) polypeptide or nucleic acid;
  - (b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
  - (c) detecting a test agent-biased determining the activity of the assay system in the presence or absence of the test agent[.]; and
  - (d) wherein a difference between the test agent-biased activity and the reference activity identifies identifying the test agent as a candidate RB pathway modulating agent by detecting a difference in the activity of the assay system in the presence or absence of the test agent.
2. (Currently amended) The method of Claim 1, wherein the assay system comprises cultured cells that express the PSMC PSMC2 polypeptide.
3. (Currently amended) The method of Claim 2, wherein the cultured cells additionally have defective RB function.
4. (Currently amended) The method of Claim 1, wherein the assay system includes a screening assay comprising a PSMC PSMC2 polypeptide, and the candidate test agent is a small molecule modulator.
5. (Currently amended) The method of Claim 4, wherein the assay is an ATPase assay.
6. (Currently amended) The method of Claim 1, wherein the assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. (Currently amended) The method of Claim 1, wherein the assay system includes a binding assay comprising a PSMC PSMC2 polypeptide and the candidate test agent is an antibody.

8. (Currently amended) The method of Claim 1, wherein the assay system includes an expression assay comprising a PSMC PSMC2 nucleic acid and the candidate test agent is a nucleic acid modulator.

9. (Currently amended) The method of Claim 8, wherein the nucleic acid modulator is an antisense oligomer.

10. (Currently amended) The method of Claim 8, wherein the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO).

11. (Currently amended) The method of Claim 1 additionally comprising:  
(~~d~~) (c) administering the candidate RB pathway modulating agent identified in (~~e~~)  
(d) to a model system comprising cells defective in RB function and[[,]] detecting a phenotypic change in the model system that indicates that the RB function is restored.

12. (Currently amended) The method of Claim 11, wherein the model system is a mouse model with defective RB function.

13. (Withdrawn) A method for modulating a RB pathway of a cell comprising contacting a cell defective in RB function with a candidate modulator that specifically binds to a PSMC polypeptide, whereby RB function is restored.

14. (Withdrawn) The method of Claim 13 wherein the candidate modulator is administered to a vertebrate animal predetermined to have a disease or disorder resulting from a defect in RB function.

15. (Withdrawn) The method of Claim 13 wherein the candidate modulator is selected from the group consisting of an antibody and a small molecule.

16. (Currently amended) The method of Claim 1, comprising the additional steps of:

- (e) providing a secondary second assay system comprising cultured cells or a non-human animal expressing PSMC PSMC2, wherein the second assay is capable of detecting a change in the RB pathway;
- (f) contacting the secondary second assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and
- (g) detecting an agent-biased activity of a change in the second assay system in the presence or absence of the test agent, wherein a difference between the agent-biased activity and the reference activity of change in the second assay system confirms the test agent or agent derived therefrom as a candidate RB pathway modulating agent, and wherein the second assay detects an agent-biased change in the RB pathway.

17. (Currently amended) The method of Claim 16, wherein the secondary second assay system comprises cultured cells.

18. (Currently amended) The method of Claim 16, wherein the secondary second assay system comprises a non-human animal.

19. (Currently amended) The method of Claim 18, wherein the non-human animal mis-expresses a RB pathway gene.

20. (Withdrawn) A method of modulating RB pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a PSMC polypeptide or nucleic acid.

21. (Withdrawn) The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the RB pathway.

22. (Withdrawn) The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. (Withdrawn) A method for diagnosing a disease in a patient comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with a probe for PSMC expression;
- (c) comparing results from step (b) with a control;
- (d) determining whether step (c) indicates a likelihood of disease.

24. (Withdrawn) The method of Claim 23 wherein said disease is cancer.

25. (Withdrawn) The method according to Claim 24, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.